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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,019	09/21/2001	Chikara Aizawa	SHIM1120	9316

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EXAMINER	
LE, EMILY M	
ART UNIT	**PAPER NUMBER**
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/830,019	AIZAWA ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 012/11/2006

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-3 and 7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3 and 7 is/are rejected.

7)☒ Claim(s) 2 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 4-6 and 8-15 are cancelled. Claims 1-3 and 7 are pending and under examination.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Germanier et al.,[1] as evidenced by Carson et al.[2]

In response to the art rejections, Applicant submits that the claimed attenuated toxin is produced by directly treating cholera toxin with formalin, rather than treating procholeragenoid with formalin.

Applicant's submission has been considered, however, it is not found persuasive. While it is noted that Applicant submits that claimed attenuated toxin is produced by directly treating cholera toxin with formalin, however, it should be noted that the claimed invention remains to be the purified and attenuated toxin. The claimed invention is not limited to purified and attenuated toxin produced by any particular method that would render it different from the prior art. Hence, the submission is not found persuasive.

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[1] Germanier et al. Preparation of a purified antigenic cholera toxoid. Infection and Immunity, 1976, Vol. 13, No. 6, 1692-1698.
[2] Carson et al. U.S. Patent No. 6610661.

In addition to above, Applicant submits that Germainer et al. is silent on the adjuvant activity of the attenuated procholeragenoid.

Applicant's submission has been considered, however, it is not found persuasive. In the instant case, the invention remains to be the purified and attenuated toxin that can be used as an adjuvant. In the instant case, the recitation "adjuvant" does not further limit the claimed invention. The recitation "adjuvant" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Applicant further submits that Germainer does not disclose that the procholeragenoid retains an activity to enhance production of an antibody specific to an antigen other than procholeragenoid itself, e.g., having adjuvant activity.

Applicant's submission has been considered, however, it is not found persuasive. In the instant case, Germainer et al. teaches a purified and attenuated cholera toxin having residual toxic activity of less than 1/2000 of that of the corresponding toxin, which retains the natural serine, glutamic acid residues, and lysine residues of the natural toxin, and the purified and attenuated toxin has been treated with formalin. The purified and attenuated cholera toxin of Germainer et al. encompasses all the structural requirements that are recited in the claims. It is further noted that the purified and attenuated cholera toxin of Germainer et al. is indistinguishable from that of the claimed

purified and attenuated cholera toxin. Hence, the purified and attenuated cholera toxin of Germainer et al. would necessarily have the same activity as that of the claimed invention, adjuvant properties, which can be further evidenced by the Carson et al. [Lines 24-26, column 10.] At the cited passage, Carson et al. recognizes the adjuvant activity of the purified and attenuated cholera toxin discussed in Germainer et al.

Furthermore, MPEP § 2112 provides that "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Germanier et al., as applied to claim 1.

The claim limits the residual toxic activity of **less than** 1/10000.

The significance of Germanier et al. as it pertains to claim 7 is discussed above.

The difference between the claimed invention and Germanier et al. is: The residual toxic activity of the purified and attenuated cholera toxin of Germanier et al. is

noted to be 1/10000 that of its natural toxin. [Abstract] It is not readily apparent if the purified and attenuated cholera toxin of Germanier et al. is has a residual toxic activity of **less than** 1/10000 than its natural toxin.

However, MPEP § 2144.05 [R3] [II] states: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re

Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

In the instant, the specification does not contain any evidence indicating that the claimed level of toxicity is critical. Additionally, the general conditions of the claimed invention are disclosed by Germanier et al. Germainer et al. teaches the detoxification of the cholera toxin. Germainer et al. also suggests the administration of the detoxified toxin with whole cell vaccines against *Vibrio cholerae* infection. [First sentence, third paragraph, left column, page 1692] Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to reduce the toxicity of the toxin to a level that ensure its safe use with whole cell vaccines against *Vibrio cholerae* infection.

6. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Germainer et al., as applied to claim 1, in view of Douce et al.[3]

Claim 2, which depends on claim 1, requires the purified and attenuated toxin to be a mutant, wherein one ore more amino acid residues are substituted, inserted, deleted or added, and having adjuvant activity, while the existing serine, glutamic acid and lysine residues are retained.

As provided above, Germainer et al. teaches the purified and attenuated toxin of claim 1. However, Germainer et al. does not teach the substitution, insertion, deletion or addition of one or more amino acid residues of the purified and attenuated toxin.

However, Douce et al. teaches the substitution, insertion, deletion or addition of one or more amino acid residues of a toxin to modify the adjuvanticity and

immunogenicity of the toxin while retaining the existing serine, glutamic acid and lysine residues.

Hence, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to have combine the teachings of Douce et al. and Germainer et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to modify the adjuvanticity and immunogenicity of the purified and attenuated toxin of Germainer et al. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because Douce et al. teaches the modification of immunogenicity and adjuvanticity of a toxin by introducing mutation in the amino acid sequence of the mutant.

Conclusion

7. No claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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[3] Douce et al. Intranasal immunogenicity and adjuvanticity of site-directed mutant derivatives of cholera

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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toxin. Infection and Immunity, Vol. 65, No. 7,2821-2828.